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Chronic Fatigue Syndrome

MEDICINE FOR THE PUBLIC

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Foreword

Americans continue to demand a greater role in deciding issues that affect their health. Increased health awareness and the convincing evidence linking lifestyle, risk factors and specific diseases have accelerated our need to know.

The Clinical Center, recognizing the importance of providing information to facilitate intelligent decisions on health issues, created a unique lecture series featuring physician scientists working at the frontiers of biomedical research at the National Institutes of Health.

The Medicine for the Public series has provided an opportunity for thousands of people to learn more about how their bodies work and what they can do to maintain or improve their health.

This publication is one of several adapted from the series. It is our sincere hope that you will find this material interesting and enlightening.

Saul Rosen, Ph.D., M.D.
Acting Director
Warren Grant Magnuson Clinical Center
National Institutes of Health

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THE SYMPTOMS, NATURE, CAUSES, AND CURE OF THE FEBRICULA, OR LITTLE FEVER:

COMMONLY CALLED

The NERVOUS or HYSTERIC Fever; the *Fever* on the SPIRITS; VAPOURS, HYPO, or SPLEEN.

BY

Sir RICHARD MANNINGHAM, Knt.
M.D. F.R.S. and of the College of Physicians, LONDON.

FEBRIUM *omnium* Aer *Auctor existit.*
HIPPOCRATES, Art. *de Aere.*

NATURA, *dum in* PERSPIRANDI *officio est impedita, incipit statim in* Multis *deficere.*
SANCTORIUS.

SECOND EDITION with ADDITIONS.

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Chronic Fatigue Syndrome

About the Syndrome

Tired. Exhausted. Worn down. There are times when we've all felt such fatigue, when we don't want to go back to work for a week or two, or wish we could have a month off to rest. But chronic fatigue syndrome differs from the more typical feelings of fatigue; it is a debilitating disorder that interferes with a person's ability to participate in the activities of daily life, sometimes for long periods of time. Even the simplest task can become a hurdle to overcome, and expending just a small amount of energy can put a person right back in bed.

Some of the symptoms of chronic fatigue syndrome are constant tiredness and feeling easily exhausted. There may also be recurring dull headaches; joint and muscle aches; a feeling of feverishness and chills without high fever; depression; difficulty in concentrating on tasks; and tender lymph glands. Of course, many of these symptoms also occur as part of other illnesses, making chronic fatigue syndrome difficult to diagnose and to categorize.

History

Although the syndrome has only recently been publicized, it isn't new, and it's probably not increasing in frequency. However, the name, chronic fatigue syndrome, is new. Researchers chose the name because they believe this illness is not a single disease, but results from a combination of several factors. In addition, the name accurately describes the characteristic problems of the disorder without second guessing the underlying causes. Every time someone has tried to pinpoint a cause in the past, they've been mistaken.

A textbook written in 1750 by an English physician, Sir Richard Manningham, described symptoms of a disease he calls "febricula," or "little fever," which sound strikingly similar to those of chronic fatigue syndrome. People in that era also referred to an illness called "the vapors," characterized by great fatigue.

As early as 1871, physicians began diagnosing exhaustion in soldiers following the stress of battle. This version of fatigue syndrome became known as "soldier's heart," or "the effort syndrome." During World War I some 60,000 of the British forces were diagnosed with the problem and 44,000 of these were retired from the military because they could no longer function in combat.

In 1934, an American physician, Alice Evans, suggested that chronic fatigue was caused by a bacterial infection transmitted through farm animals. She called the illness "chronic brucellosis." In that same year, there was an outbreak of a strange illness called "benign myalgic encephalitis," so named because it involved both impairment in brain function and muscle pain.

During the 1970's people equated the fatigue syndrome with hypoglycemia, or low blood sugar. But, in fact, people with chronic fatigue syndrome do not typically have low blood sugar. Among other possible culprits people suspected might cause chronic fatigue were Candida, a yeast, and the Epstein Barr virus, a type of herpes virus that causes mononucleosis, or "the kissing disease." There is no clearcut evidence, however, that any of these are the primary cause of the syndrome.

Another possible, but still unproven, theory is that severe allergies can trigger chronic fatigue syndrome; some people who believe this theory would rather call the resulting disorder "total allergy syndrome."

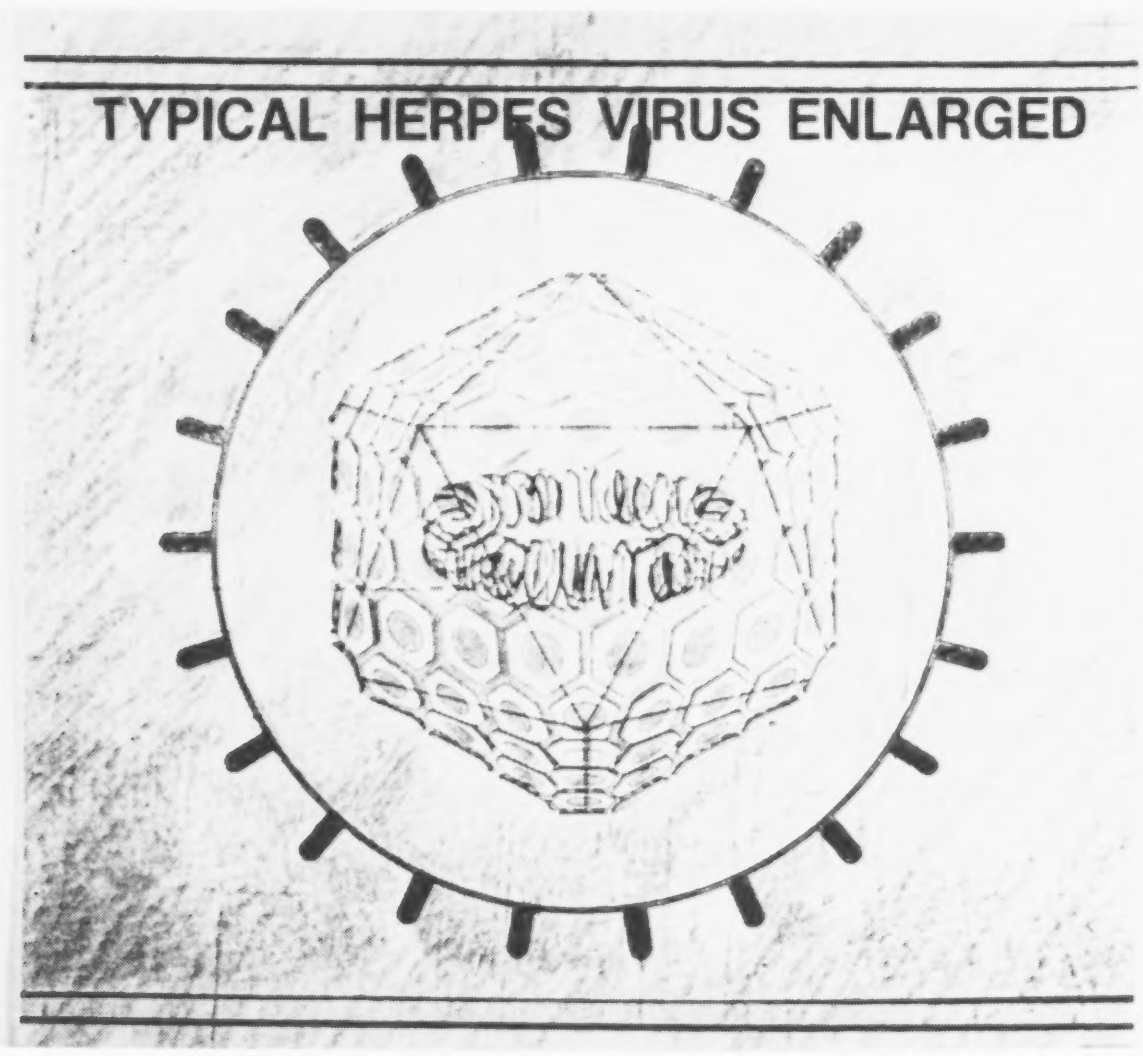
At least two-thirds of the people with chronic fatigue syndrome are women; most are middle-class and white. So there appears to be risk factors among race, sex and socioeconomic status that can predispose a person to chronic fatigue syndrome, although we do not understand the reasons for these factors.

Most people with chronic fatigue syndrome relate the onset of the illness to a particular infection, one that they might have had before without such long-lasting consequences. These infections, which at first do not seem severe, most often include respiratory or gastrointestinal illness, flu-like disease, bronchitis, sore throats, colds or diarrhea, mononucleosis, hepatitis or jaundice. The vast majority of people recover completely from these illnesses, but a small percentage are left feeling extremely weak, tired and depressed, long after the main symptoms of the infections have vanished. These fatigue-related symptoms

can linger. Even so they usually resolve by themselves, but if they persist for more than six months the person may have the chronic fatigue syndrome.

During the early months of fatigue, the patient may feel like he or she is on a medical merry-go-round, going from specialist to specialist in search of what's wrong. An allergist might refer the patient to a neurologist, a neurologist might refer him or her to a psychiatrist. Some patients may benefit from a psychological evaluation and anti-depressant therapy, some do not. And some might be further frustrated by a psychiatrist who determines that the problem is not related to emotional stress or conflict. Right now, established medicine has not provided adequate direction for such patients, who are unsure of where to seek help.

Some patients have formed support groups for chronic fatigue syndrome. These groups—which now exist throughout the United States, Canada, Western Europe and Australia—disseminate information on the illness and provide comfort. People recognize they are not alone in dealing with this still mysterious disease. Other people turn to a more individual approach. Some turn to meditation,



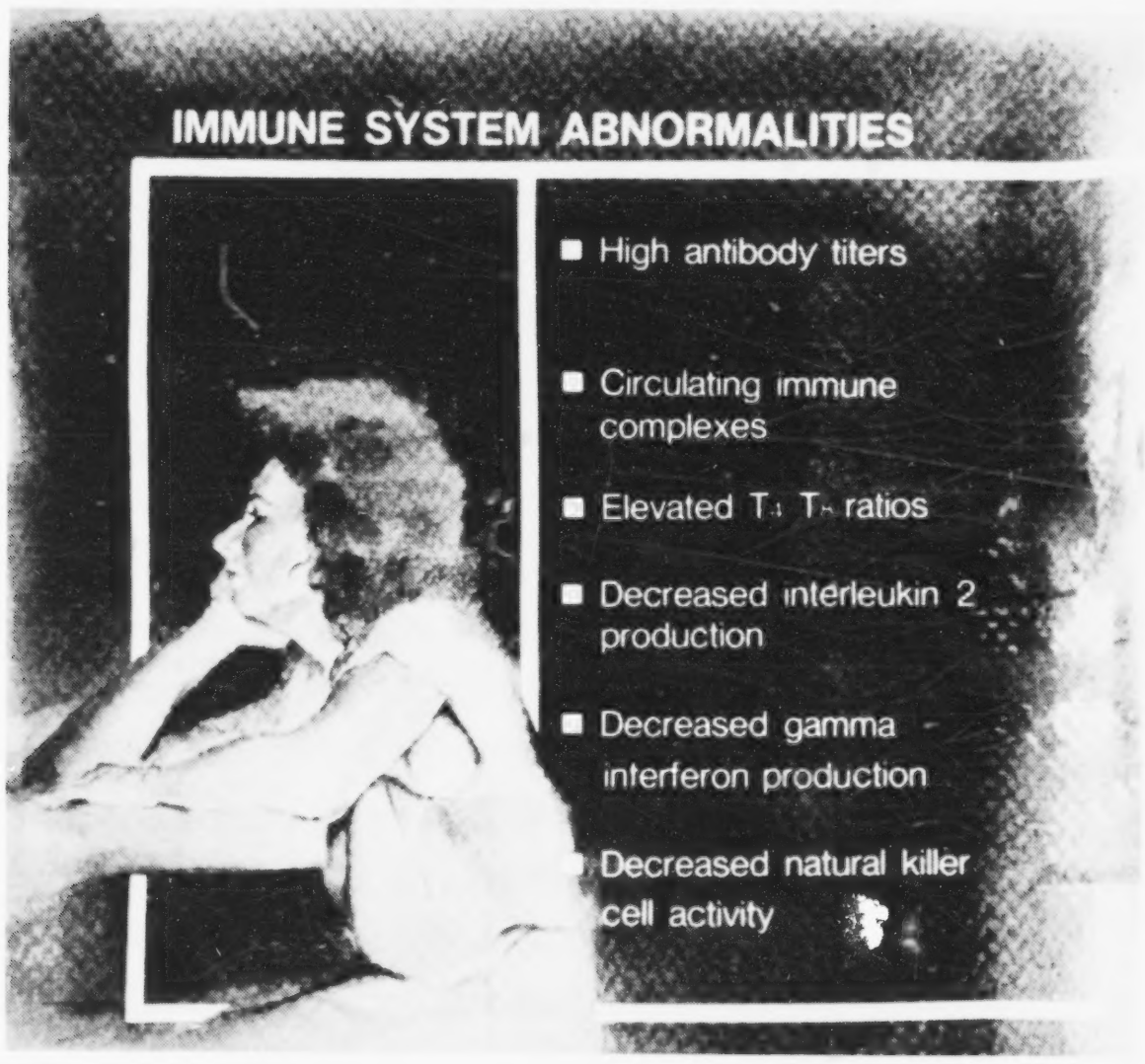
acupuncture or acupressure, as well as homeopathic or other non-traditional therapies.

But what can medical science offer, besides an analysis of risk factors for the illness? So far, investigators are still learning the basic facts. Researchers now recognize that chronic fatigue syndrome could be composed of many elements. One element may be an infection that triggers the initial illness and could even linger in the body to cause recurring symptoms over long periods. Viruses with this ability include the herpes viruses. This family of viruses contains a protective shell, inside which resides genetic information that allows the infectious agent to persist in the body for life.

Some people with chronic fatigue syndrome do, in fact, have high levels of antibodies to the Epstein-Barr virus, indicating they had experienced a previous infection with it and perhaps recurrent infections as well. But other people with the syndrome have normal or no antibodies to the virus, so that Epstein-Barr virus may not be that important after all. Other evidence that the Epstein-Barr virus is not directly linked to chronic fatigue syndrome comes from studies with a drug called acyclovir, which blocks the virus' multiplication. Patients with chronic fatigue syndrome treated with the drug did not show significant improvement compared to those given a placebo. So, the search for the infectious agent(s) that may trigger the syndrome continues.

Another common factor in chronic fatigue syndrome is allergy. Patients have twice the number of allergic skin reactions as people without the illness. We don't know why this is so, but this information may indicate that the patients may be overly sensitive to certain agents. Such extra sensitivity may predispose the patients to infections or other types of abnormal reactions to foreign substances and might account for the syndrome.

What do we know about the immune system in people with chronic fatigue syndrome? Several studies have revealed that certain components of the immune system behave



abnormally. For example, chemicals called interleukin-2 and gamma interferon, which the body produces during its battle against cancer and infectious agents, may not be made in normal amounts. Natural killer cells that also help the body in this battle are found in slightly reduced numbers. The reduction in natural killer cell activity is very small, and the affected cells comprise just a tiny portion of the immune system. Nevertheless, this subset of cells does tend to have lower activity in people with chronic fatigue syndrome.

It's important to note that another syndrome has the identical, small reduction in natural killer cell activity. That syndrome is clinical depression. Depressed patients have reduced natural killer cell activity and slightly decreased interferon production. In addition, some depressed patients produce higher amounts of antibodies to certain viruses. We don't know why. Therefore, there may be more of a

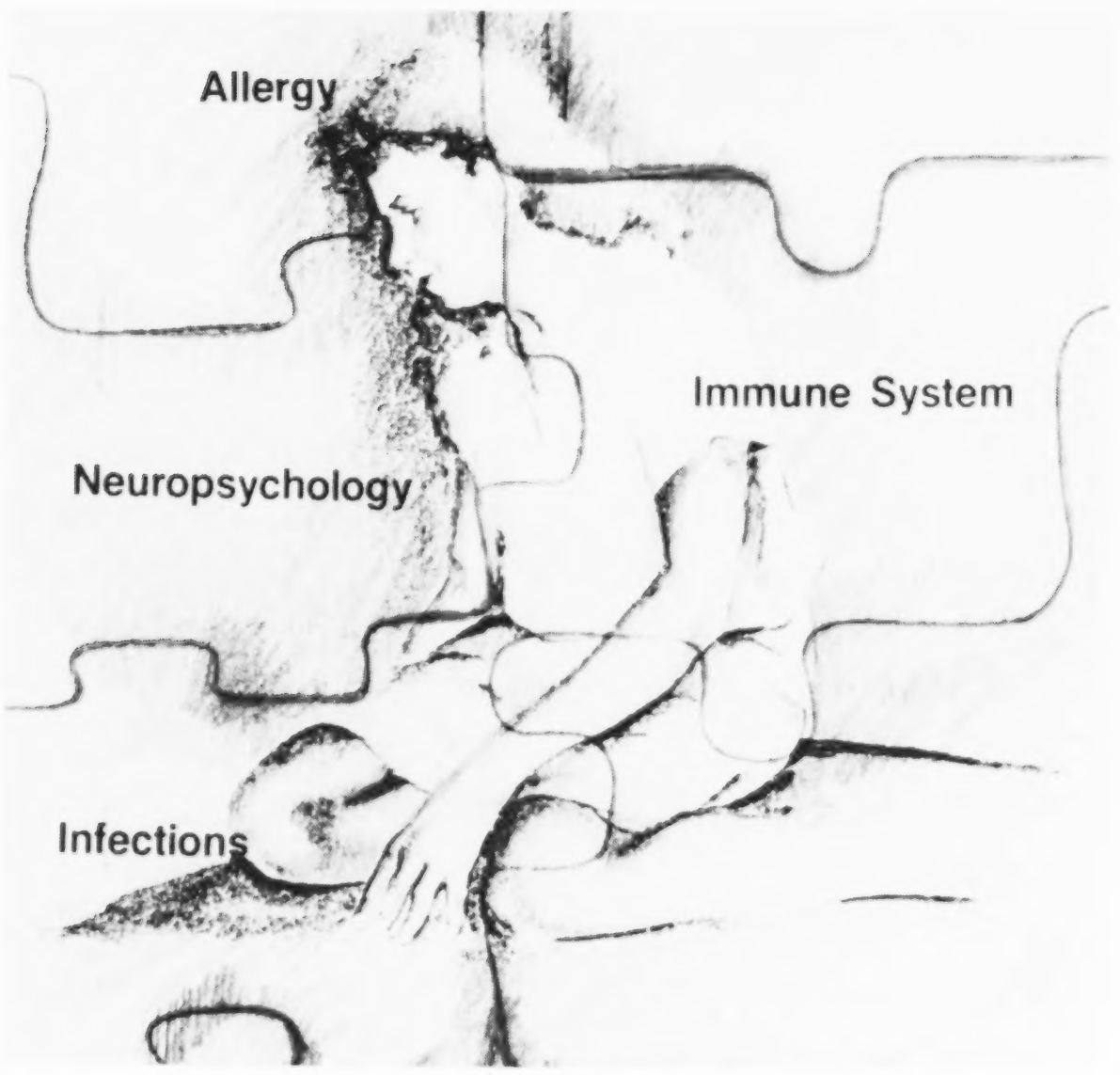
connection between depression, the immune system and the chronic fatigue syndrome than is realized even now.

This brings us to one of the most difficult and controversial aspects of the syndrome, its neuropsychological features. As already described, many of the patients are depressed. But the most common complaint of patients is that they can't concentrate, whether it's an attempt to get their work done or wash the dishes. They also can't remember what they have to do to complete a task. Psychologists at the National Institutes of Health and other research institutions are trying to measure such deficits in concentration and memory, and to determine if the impairment can predict risk or help diagnose someone with the syndrome.

In addition to the role that an acute infection may play in triggering chronic fatigue syndrome, many patients report that the onset of the syndrome occurs at a time of great stress, such as a divorce, job change, moving, or a death in the family. These traumatic events seem to predate chronic fatigue syndrome by a matter of weeks or a few months. What role could stress play in triggering the syndrome? We don't know the answer to that, but several studies, including some dating back to the 1950s, show a correlation between stress and reduced ability to recover from illness. Other studies show that people under stress may be more susceptible to infection.

In summary, researchers believe that the likelihood of developing chronic fatigue syndrome is enhanced by a combination of factors, including an acute infection and the neuropsychological makeup of the individual. The syndrome, then, appears to be a problem that requires an interdisciplinary team of physicians, allergists, psychologists, immunologists and others to tackle. Together, we are searching for the unifying thread that can fully explain and allow us to better treat chronic fatigue syndrome.

In the meantime, physicians can perform tests to rule out other illnesses, many of which require other treatments. And patients can take comfort in knowing that the syndrome they suffer from is not life-threatening, and that most of them will improve with time. The headaches, muscle aches and joint aches can be treated with aspirin, Tylenol or other anti-inflammatory drugs; adjustments in diet or short-term medication may enable many to sleep through the night. Some individuals may find that anti-depressants enable them to cope with their debilitating illness and feel stronger. In addition to medical treatment, however, both the family and the patient need better guidance about the syndrome. Right now, we don't know exactly what to advise patients. But new research may remove that uncertainty and provide the tools for determining the best way to treat the syndrome and counsel those who are sick.



Questions and Answers

Q. Does chronic fatigue syndrome worsen over time?
A. The pattern of this illness establishes itself very early, although there are some fluctuations. Most people with the syndrome do eventually get better, and we have not seen anyone deteriorate to a more physically devastating, or terminal, illness.

Q. I think I have the syndrome. Where can I go for a definitive diagnosis?
A. There is no definitive blood test or other diagnostic test. Rheumatologists, immunologists, specialists in infectious diseases, psychologists and allergists all have their own interpretations, but the facts aren't all in yet, and we have no objective test.

Q. Do people with the syndrome have heart palpitations or abnormal body temperature?
A. Some patients do have palpitations. In fact, the syndrome in the 1870s was know as "soldier's heart." But we don't find that the palpitations typically require anti-arrhythmic drugs or other medication. To answer the second part of your question, many people with the syndrome complain of running higher or lower temperatures than normal. As part of our acyclovir study, we took thousands of measurements of body temperature and found no significant abnormalities.

Q. Is shortness of breath a symptom of chronic fatigue syndrome?

A. Shortness of breath can occur in anyone who is severely deconditioned and then tries to do even light exercise. But abnormal lung function or low concentration of oxygen in the blood at rest are not a feature of the syndrome.

Q. I have had laboratory tests that indicate I have chronic infection with Epstein-Barr virus. Does this mean I have chronic fatigue syndrome?

A. No. We have found no definite correlation between Epstein-Barr infection and the syndrome; most people have antibodies to the virus so the tests are probably irrelevant for diagnosing chronic fatigue syndrome.

Q. Are antidepressants a treatment for chronic fatigue syndrome?

A. These drugs may be useful. Some people believe the tricyclic group of antidepressants is better, while others think monoamine oxidase inhibitor antidepressants may have more benefit. It's too soon to say which class of antidepressants is more effective, but this is an area of active study. We are also trying to determine the optimal dose of these drugs for people with the syndrome; some individuals are very sensitive to what may be a moderate or low dose in other patients. And these patients can feel worse if the dose becomes too large.

Q. Can a person's level of natural killer cells be restored if it's abnormally low?

A. First of all, it's not clear if such a deficiency actually contributes to the symptoms or causes of chronic fatigue syndrome. And even if there is a correlation, these deficiencies may predate the syndrome by several years. But there are experimental ways to boost natural killer cell activity. In certain illnesses other than chronic fatigue syndrome, we do this by giving people injections of interferon, a vital component of the immune system. We are reluctant to give such injections for people with the syndrome because interferon itself causes fever, fatigue, exhaustion, muscle aches and headaches. We might, in fact, end up worsening the existing symptoms of the syndrome.

Q. When or how often do recurrent episodes of fatigue or illness occur in someone with chronic fatigue syndrome?
A. The pattern varies from individual to individual. Some people are ill all the time, some are well except for a single fatigue episode every several weeks. We just can't predict what will happen.

Q. Is impairment of thyroid activity related to chronic fatigue syndrome?
A. There are two issues about the thyroid that are relevant here. One is that all patients who undergo evaluation for the syndrome should have a thyroid test, because an overly or underly active thyroid can produce many of the same symptoms, particularly exhaustion. If they have abnormal thyroid activity, we treat them for thyroid disease, and these people respond well to the treatment. Secondly, some patients with chronic fatigue syndrome have antibodies to thyroid proteins, but it is unclear whether that causes thyroid disease. That's a question that's still under study.

Q. I would like to know if meditation or yoga might be an answer for people with chronic fatigue syndrome. I know it helps me when I feel exhausted.

A. I think anything that reduces stress and makes someone feel more comfortable can help with a lot of illnesses. But I don't know whether meditation is an adequate treatment for this syndrome. The best I can say now is that it can't hurt, and it may help.

Biography

Stephen Straus received his medical degree from the College of Physicians and Surgeons of Columbia University in New York, and completed training in internal medicine and infectious diseases at Barnes Hospital in St. Louis. His work as a virologist for the past 11 years at the National Institutes of Health has led to the publication of more than 130 papers, mostly dealing with the molecular biology and treatment of human herpesvirus infections. Dr. Straus received the Public Health Service Outstanding Service Medal in 1987 and has served as a peer reviewer for many professional journals, including the *New England Journal of Medicine, Annals of Internal Medicine,* and the *Journal of the American Medical Association.* Dr. Straus has studied chronic fatigue syndrome for more than a decade.